

# Pre-Clinical and Clinical Trials Supported by the National Cancer Institute

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# Outline

- Overview of NCI supported research by mechanism
  - Grants
  - Contracts
  - Cooperative Groups / Consortia
- Radioisotope use in Grants portfolio
- Contract space
- Future projects
  - NCI Intramural Use

# NCI Support Mechanisms Overview

Grants (R01, R21, etc)

SBIR, Academic/Industrial Partnerships

**BASIC  
RESEARCH**

**DRUG  
DISCOVERY**

**PRE-  
CLINICAL**

**CLINICAL TRIALS**

**PHASE I**

**PHASE II**

**PHASE III**

Early Phase Clinical Trials Network (ETCTN)

National Clinical Trials Network (NCTN)

NCI Experimental Therapeutics Program (NExT)

# Radioisotope Use in NCI Grants Portfolio

- QVR search of grants
- Institute: NCI
- Funded projects only
- Competing projects only (no renewals)
- Time frame: 2012-2016 (past 5 years)
- Search terms via RCDC (Research, Condition, and Disease Categorization) indexed terms

# Grant Portfolio Results

Search Terms	Number of Awards	Total Funding
Radionuclide Therapy or Radioimmunotherapy	30	\$8.1M
Radiopharmaceuticals	58	\$14.5M
Radioisotopes	125	\$33.2M
All 3 above	161	\$42.8M
All 3 above (including non-funded)	1009 applications	\$42.8M
All 3 above (including non-NCI)	307	\$91.1M
All 3 above (including non-NCI and non-funded)	1859 applications	\$91.1M

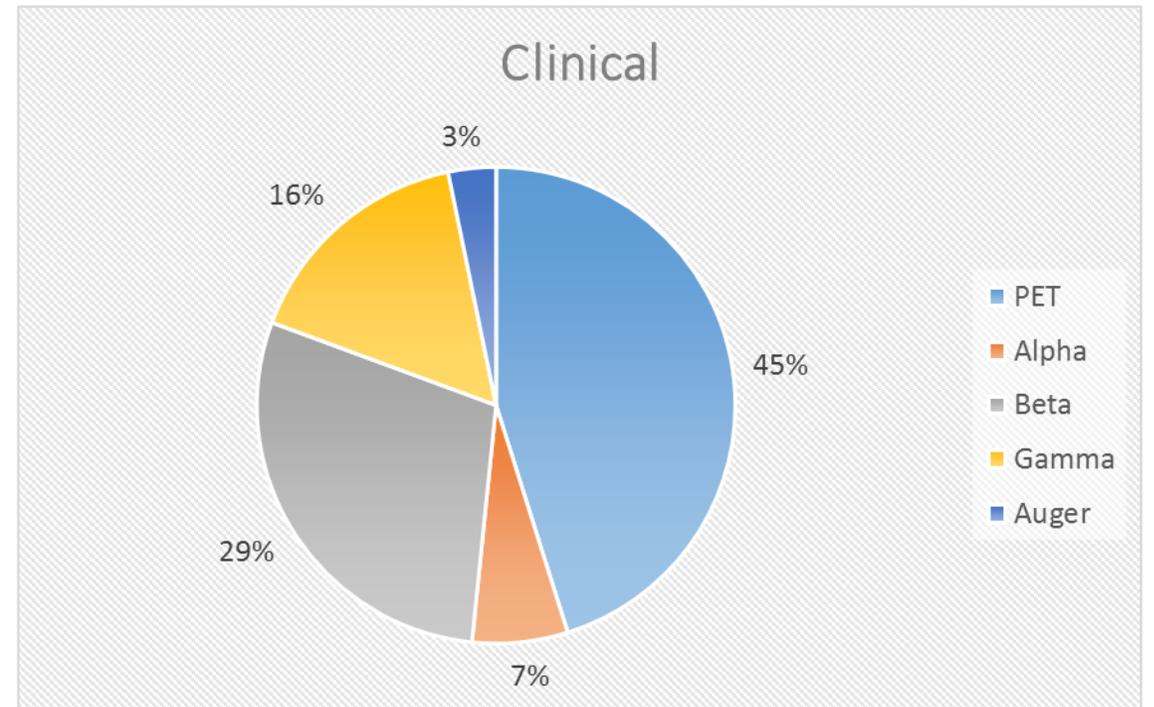
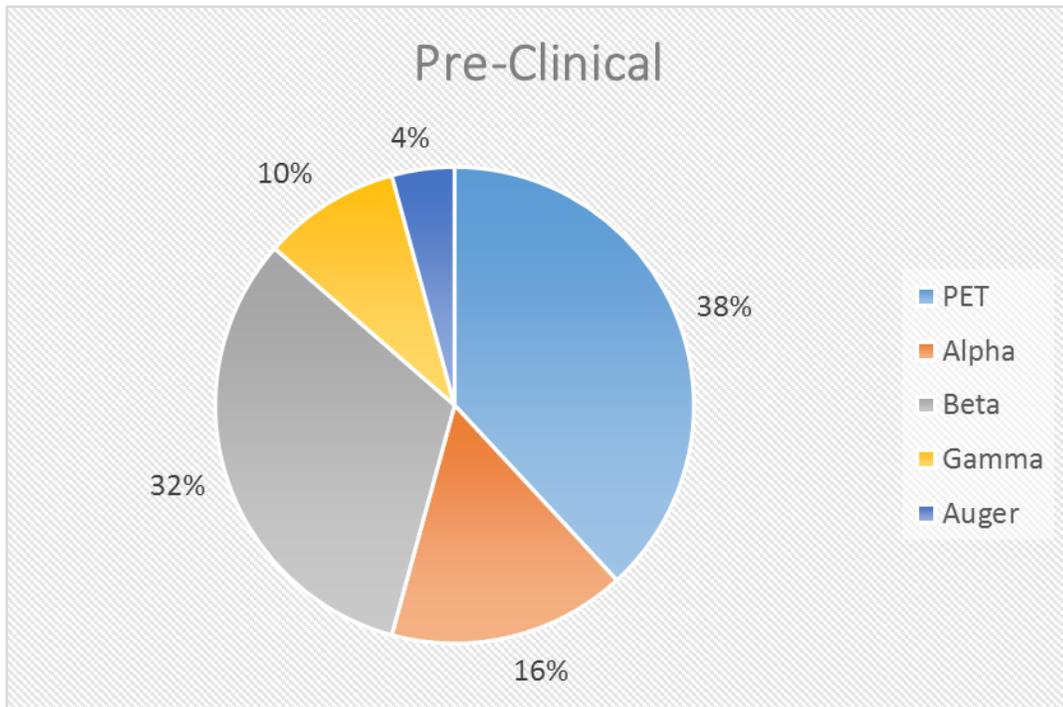
# NCI-Only Funded Grants

- 161 awards for \$42.8M
- Pre-clinical: 107 vs. Clinical: 49 (5 exempt studies)
- Wide range of radio-isotopes used in pre-clinical studies
- Limited variety for human studies

# Radio-isotope Use in NCI Grant Portfolio

Isotope	Pre-Clinical	Clinical	Isotope	Pre-Clinical	Clinical
<sup>62</sup> Cu	0	1	<sup>153</sup> Sm	1	1
<sup>64</sup> Cu	5	2	<sup>223</sup> Ra	1	0
<sup>86</sup> Y	2	0	<sup>205/206</sup> Bi	1	0
<sup>90</sup> Y	11	6	<sup>212</sup> Bi	3	0
<sup>103</sup> Pd	1	1	<sup>213</sup> Bi	2	0
<sup>177</sup> Lu	11	1	<sup>11</sup> C	1	0
<sup>68</sup> Ga	2	3	<sup>211</sup> At	6	2
<sup>123</sup> I	2	0	<sup>32</sup> P	2	0
<sup>124</sup> I	4	1	<sup>203</sup> Pb	5	0
<sup>125</sup> I	4	1	<sup>212</sup> Pb	8	0
<sup>131</sup> I	7	1	<sup>225</sup> Ac	4	0
<sup>166</sup> H	1	0	<sup>111</sup> In	1	1
<sup>89</sup> Zr	11	3	<sup>153</sup> Gd	1	0
<sup>99m</sup> Tc	2	3			
<sup>18</sup> F	15	4			

# Radio-isotope Use by Particle Emission



# Portfolio Analysis Caveats

- More focused on radionuclide in therapeutic setting
- If use “PET Imaging” as search term:
  - 303 awards for \$84.5M
  - Have a lot more  $^{89}\text{Zr}$ ,  $^{18}\text{F}$ ,  $^{68}\text{Ga}$
  - Some more  $^{64}\text{Cu}$ ,  $^{11}\text{C}$

# Radio-isotope Use in NCI SBIR Contracts

- Agents that have been identified as high scientific impact and chosen for significant funding with commercialization as goal
- 14 funded projects: \$300k for first 9 months, then \$2M for 2 years

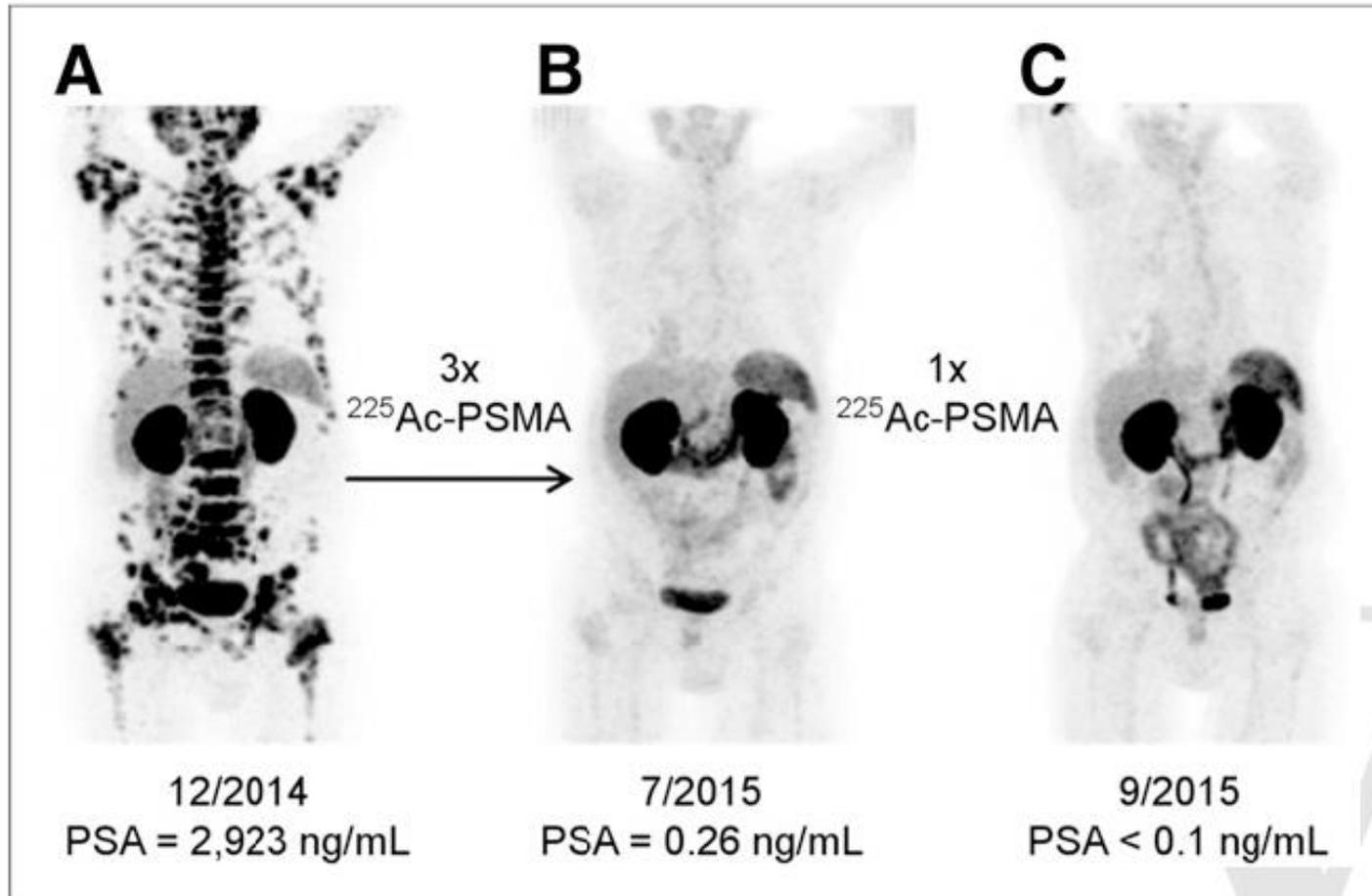
Isotope	Projects	Isotope	Projects
$^{203}\text{Pb}/^{212}\text{Pb}$	2	$^{68}\text{Ga}/^{177}\text{Lu}$	1
$^{18}\text{F}$	2	$^{89}\text{Zr}$	2
$^{124}\text{I}$	1	$^{222}\text{Ac}/^{225}\text{Ac}$	1
$^{131}\text{I}$	3	$^{86}\text{Y}/^{90}\text{Y}$	1

# Alpha particle RNT with PSMA Agents

**TABLE 1**  
Overview of Pretreatments

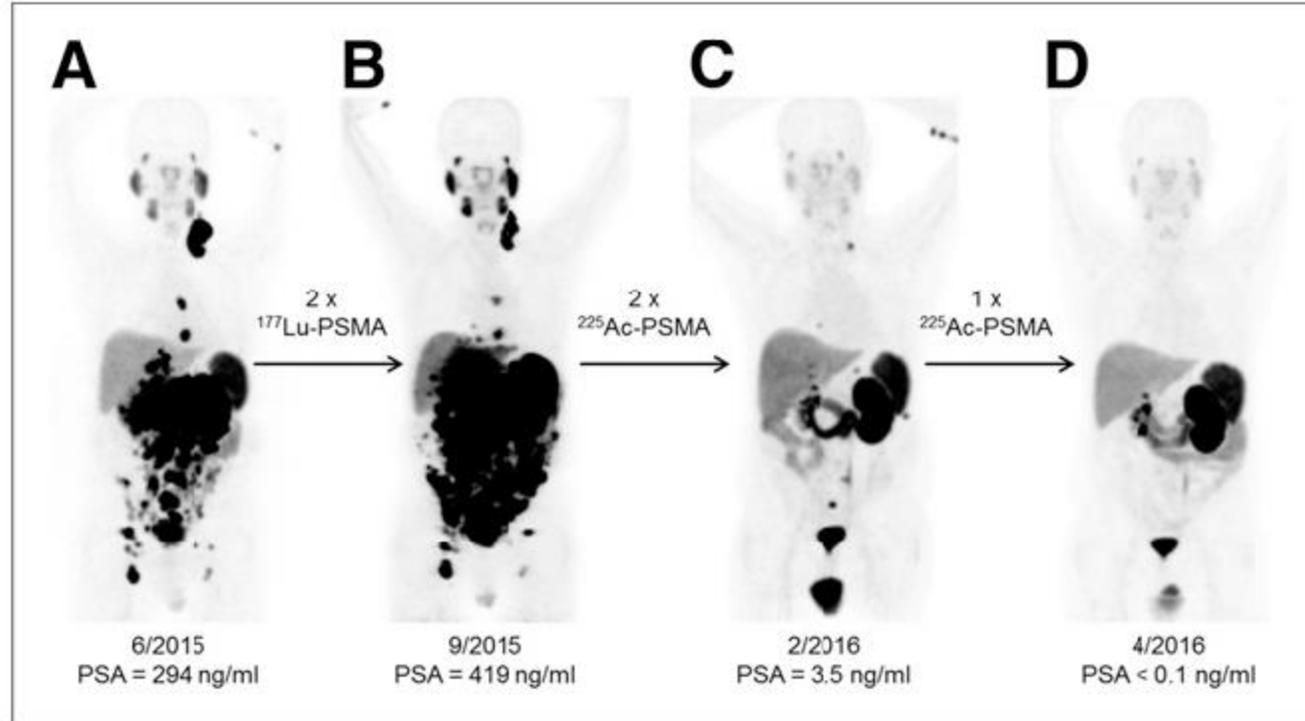
Patient A	Patient B
Leuprorelin	Radical prostatectomy
Zoledronate	Radiotherapy of lymph node metastasis
Docetaxel (50 cycles)	Leuprorelin
Carmustine/epirubicin in hyperthermia	Leuprorelin plus bicalutamide, 150 mg/d
Abiraterone	Docetaxel (11 cycles)
Enzalutamide	Cabazitaxel (10 cycles)
<sup>223</sup> Ra (6 cycles)	Abiraterone
Abiraterone reexposition	Enzalutamide (not tolerated)
Estramustine	

# Patient A



**FIGURE 1.** <sup>68</sup>Ga-PSMA-11 PET/CT scans of patient A. Pretherapeutic tumor spread (A), restaging 2 mo after third cycle of <sup>225</sup>Ac-PSMA-617 (B), and restaging 2 mo after one additional consolidation therapy (C).

# Patient B



**FIGURE 3.**  $^{68}\text{Ga}$ -PSMA-11 PET/CT scans of patient B. In comparison to initial tumor spread (A), restaging after 2 cycles of  $\beta$ -emitting  $^{177}\text{Lu}$ -PSMA-617 presented progression (B). In contrast, restaging after second (C) and third (D) cycles of  $\alpha$ -emitting  $^{225}\text{Ac}$ -PSMA-617 presented impressive response.

# Conclusions

- Wide variety of radio-isotopes being used
- PET agents are the most studied;  $\beta$ -emitters second
- Shift towards  $\alpha$ -emitters seen in pre-clinical already -> likely to carry over to clinical studies in the future